

SEQUENCE LISTING

<110> Ono et al.

<120> Modified antibodies recognizing receptor trimers or higher multimers

<130> 75996-01

<150> PCT/JP2004/018507
 <151> 2004-12-10

<150> JP 2003-415735
 <151> 2003-12-12

<160> 42

<170> PatentIn version 3.1

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 <212> DNA
 <213> Artificial

<220>
 <223> An artificially synthesized nucleotide sequence

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 ctgagactct cctgtgcagc ctctggattc acctttagca gctatgccat gagctgggtc 180
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 agatactacg cagactccgt gaagggccgg ttcaccatct ccagagacaa ttccaagaac 300
 acgctgtatc tgcaaatgaa cagcctgaga gccgaggaca cggccgtata ttactgtgcg 360
 aaagagagca gtggctgggt cggggccttt gactactggg gccagggaac cctgggtcacc 420
 gtctcctcag gtggagaaat tgtgctgact cagtctccag actttcagtc tgtgactcca 480
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 taccagcaga aaccagatca gtctccaaag ctctcatca agtatgcttc ccagtccttc 600
 tcaggggtcc cctcgagggt cagtggcagt ggatctggga cagatttcac cctcaccatc 660
 aatagcctgg aagctgaaga tgctgcagcg tattactgtc atcagagtag tagtttaccg 720
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<212> PRT

<213> Artificial

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Val Gln Cys Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Arg Tyr Tyr Ala
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Lys Glu Ser Ser Gly Trp Phe Gly Ala Phe Asp Tyr
115 120 125

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Glu Ile Val
130 135 140

Leu Thr Gln Ser Pro Asp Phe Gln Ser Val Thr Pro Lys Glu Lys Val
145 150 155 160

Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Gly Ser Ser Leu His Trp
165 170 175

Tyr Gln Gln Lys Pro Asp Gln Ser Pro Lys Leu Leu Ile Lys Tyr Ala
180 185 190

Ser Gln Ser Phe Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
195 200 205

Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
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Ala Ala Tyr Tyr Cys His Gln Ser Ser Ser Leu Pro Ile Thr Phe Gly
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Gln Gly Thr Arg Leu Glu Ile Lys Asp Tyr Lys Asp Asp Asp Asp Lys
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 cgccaggctc caggggaaggg gctggagtgg gtctcagcta ttagtggttag tggtagtagc 240
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 ggggtcccct cgaggttcag tggcagtgga tctgggacag atttcaccct caccatcaat 660
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 Val Gln Cys Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln
 20 25 30
 Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
 35 40 45
 Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu

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Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Arg Tyr Tyr Ala 65 70 75 80		
Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn 85 90 95		
Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val 100 105 110		
Tyr Tyr Cys Ala Lys Glu Ser Ser Gly Trp Phe Gly Ala Phe Asp Tyr 115 120 125		
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Glu Ile Val Leu 130 135 140		
Thr Gln Ser Pro Asp Phe Gln Ser Val Thr Pro Lys Glu Lys Val Thr 145 150 155 160		
Ile Thr Cys Arg Ala Ser Gln Ser Ile Gly Ser Ser Leu His Trp Tyr 165 170 175		
Gln Gln Lys Pro Asp Gln Ser Pro Lys Leu Leu Ile Lys Tyr Ala Ser 180 185 190		
Gln Ser Phe Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly 195 200 205		
Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala 210 215 220		
Ala Tyr Tyr Cys His Gln Ser Ser Ser Leu Pro Ile Thr Phe Gly Gln 225 230 235 240		
Gly Thr Arg Leu Glu Ile Lys Asp Tyr Lys Asp Asp Asp Asp Lys 245 250 255		

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 ctgagactct cctgtgcagc ctctggattc accttttagca gctatgccat gagctggggtc 180
 cgccaggctc caggggaaggg gctggagtgg gtctcagcta ttagtggttag tggtggtagc 240
 agatactacg cagactccgt gaagggccgg ttcaccatct ccagagacaa ttccaagaac 300

acgctgtatc tgcaaatgaa cagcctgaga gccgaggaca cggccgtata ttactgtgcg 360
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gtctcctcag aaattgtgct gactcagtct ccagactttc agtctgtgac tccaaaggag 480
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cagaaaccag atcagtctcc aaagctcctc atcaagtatg cttcccagtc cttctcaggg 600
gtcccctcga gggtcagtgg cagtggatct gggacagatt tcaccctcac catcaatagc 660
ctggaagctg aagatgctgc agcgtattac tgtcatcaga gtagtagttt accgatcacc 720
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Val Gln Cys Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln
20 25 30
Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45
Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60
Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Arg Tyr Tyr Ala
65 70 75 80
Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95
Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
100 105 110
Tyr Tyr Cys Ala Lys Glu Ser Ser Gly Trp Phe Gly Ala Phe Asp Tyr
115 120 125
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Glu Ile Val Leu Thr
130 135 140
Gln Ser Pro Asp Phe Gln Ser Val Thr Pro Lys Glu Lys Val Thr Ile

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				165					170					175	
Gln	Lys	Pro	Asp	Gln	Ser	Pro	Lys	Leu	Leu	Ile	Lys	Tyr	Ala	Ser	Gln
			180					185					190		
Ser	Phe	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr
		195					200					205			
Asp	Phe	Thr	Leu	Thr	Ile	Asn	Ser	Leu	Glu	Ala	Glu	Asp	Ala	Ala	Ala
	210					215					220				
Tyr	Tyr	Cys	His	Gln	Ser	Ser	Ser	Leu	Pro	Ile	Thr	Phe	Gly	Gln	Gly
225					230					235					240
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 <212> DNA
 <213> Artificial

<220>
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cgccaggctc caggggaaggg gctggagtgg gtctcagcta ttagtggtag tggtagtagc	240
agatactacg cagactccgt gaagggccgg ttcaccatct ccagagacaa ttccaagaac	300
acgctgtatc tgcaaatgaa cagcctgaga gccgaggaca cggccgtata ttactgtgcg	360
aaagagagca gtggctgggt cggggccttt gactactggg gccagggaac cctggtcacc	420
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gtgactccaa aggagaaagt caccatcacc tgccgggcca gtcagagcat tggtagtagc	540
ttacactggg accagcagaa accagatcag tctccaaagc tcctcatcaa gtatgcttcc	600
cagtccttct caggggtccc ctgaggttc agtggcagtg gatctgggac agatttcacc	660
ctcaccatca atagcctgga agctgaagat gctgcagcgt attactgtca tcagagtagt	720
agtttaccga tcaccttcgg ccaagggaca cgactggaga ttaaaagagc tgatgctgca	780
gctgcaggag gtcccgggtc cgaggtacag ctgttggagt ctgggggagg cttggtacag	840

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tattactgtg cgaaagagag cagtggctgg ttcggggcct ttgactactg gggccaggga     1140
accctgggtca ccgtctcctc aggtggaggc ggatcggaaa ttgtgctgac tcagtctcca     1200
gactttcagt ctgtgactcc aaaggagaaa gtcaccatca cctgccgggc cagtcagagc     1260
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acagatttca ccctcaccat caatagcctg gaagctgaag atgctgcagc gtattactgt     1440
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<212> PRT

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Val Gln Cys Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln
20              25              30

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Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35              40              45

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```

Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50              55              60

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Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Arg Tyr Tyr Ala
65              70              75              80

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Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85              90              95

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Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
100             105             110

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Tyr Tyr Cys Ala Lys Glu Ser Ser Gly Trp Phe Gly Ala Phe Asp Tyr

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145					150					155				160
Glu	Lys	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Gln	Ser	Ile	Gly	Ser
				165					170				175	Ser
Leu	His	Trp	Tyr	Gln	Gln	Lys	Pro	Asp	Gln	Ser	Pro	Lys	Leu	Ile
			180					185					190	
Lys	Tyr	Ala	Ser	Gln	Ser	Phe	Ser	Gly	Val	Pro	Ser	Arg	Phe	Gly
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Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Asn	Ser	Leu	Ala
	210					215					220			
Glu	Asp	Ala	Ala	Ala	Tyr	Tyr	Cys	His	Gln	Ser	Ser	Ser	Leu	Ile
225					230					235				240
Thr	Phe	Gly	Gln	Gly	Thr	Arg	Leu	Glu	Ile	Lys	Arg	Ala	Asp	Ala
				245					250					255
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			260					265					270	Gly
Gly	Leu	Val	Gln	Pro	Gly	Arg	Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ser
		275					280					285		
Gly	Phe	Thr	Phe	Ser	Ser	Tyr	Ala	Met	Ser	Trp	Val	Arg	Gln	Pro
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Gly	Lys	Gly	Leu	Glu	Trp	Val	Ser	Ala	Ile	Ser	Gly	Ser	Gly	Ser
305					310					315				320
Arg	Tyr	Tyr	Ala	Asp	Ser	Val	Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg
				325					330					335
Asn	Ser	Lys	Asn	Thr	Leu	Tyr	Leu	Gln	Met	Asn	Ser	Leu	Arg	Glu
			340					345					350	
Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Ala	Lys	Glu	Ser	Ser	Gly	Trp	Gly
		355					360					365		
Ala	Phe	Asp	Tyr	Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Gly
						375					380			
Gly	Gly	Gly	Ser	Glu	Ile	Val	Leu	Thr	Gln	Ser	Pro	Asp	Phe	Ser
385					390					395				400
Val	Thr	Pro	Lys	Glu	Lys	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Gln
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Ile	Gly	Ser	Ser	Leu	His	Trp	Tyr	Gln	Gln	Lys	Pro	Asp	Gln	Pro

420	425	430
Lys Leu Leu Ile Lys Tyr Ala Ser Gln Ser Phe Ser Gly Val Pro Ser		
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Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn		
450	455	460
Ser Leu Glu Ala Glu Asp Ala Ala Ala Tyr Tyr Cys His Gln Ser Ser		
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Ser Leu Pro Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Asp		
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Tyr Lys Asp Asp Asp Asp Lys		
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<220>
 <223> An artificial sequence encoding linker sequence

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15

<210> 10
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 <212> PRT
 <213> Artificial

<220>
 <223> An artificially synthesized linker sequence

<400> 10
 Gly Gly Gly Gly Ser
 1 5

<210> 11
 <211> 24
 <212> DNA
 <213> Artificial

<220>
 <223> An artificial sequence encoding flag tag sequence

<400> 11
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24

<210> 12
 <211> 8

<212> PRT
 <213> Artificial
 <220>
 <223> An artificially synthesized flag tag sequence

<400> 12
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 1 5

<210> 13
 <211> 806
 <212> DNA
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<220>
 <223> An artificially synthesized diabody sequence

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 ctgagactct cctgtgcagc ctctggattc acctttagca gctatgccat gagctgggtc 180
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 acgctgtatc tgcaaatgaa cagcctgaga gccgaggaca cggccgtata ttactgtgcg 360
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 <211> 94
 <212> DNA
 <213> Artificial

<220>
 <223> An artificially synthesized oligonucleotide sequence

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gtccagtgtg aggtacagct gttggagtct gggg 94

<210> 15
<211> 96
<212> DNA
<213> Artificial

<220>
<223> An artificially synthesized oligonucleotide sequence

<400> 15
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agcctcccc agactccaac agctgtacct cacact 96

<210> 16
<211> 97
<212> DNA
<213> Artificial

<220>
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caggaagg gctggagtgg gtctcagcta ttagtg 97

<210> 17
<211> 99
<212> DNA
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<220>
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<400> 17
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<210> 18
<211> 103
<212> DNA
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<220>
<223> An artificially synthesized oligonucleotide sequence

<400> 18

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gagagccgag gacacggccg tatattactg tgcgaaagag agc 103

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ctctttcgca cagtaatata cggccgt 87

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<212> DNA
<213> Artificial

<220>
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actcagtctc cagactttca gtctgtgact ccaaagga 98

<210> 21
<211> 79
<212> DNA
<213> Artificial

<220>
<223> An artificially synthesized oligonucleotide sequence

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cacagactga aagtctgga 79

<210> 22
<211> 103
<212> DNA
<213> Artificial

<220>
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<400> 22
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ccaaagctcc tcatcaagta tgcttcccag tccttctcag ggg 103

<210> 23

<211> 97

<212> DNA

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gaggggaccc ctgagaagga ctgggaagca tacttga 97

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<211> 90

<212> DNA

<213> Artificial

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<400> 24

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gagtagtagt ttaccgatca ccttcggcca 90

<210> 25

<211> 93

<212> DNA

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<220>

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<400> 25

attgcggccg cttatcactt atcgctcgta tcctttagt ctttaatctc cagtcgtgtc 60

ccttggccga aggtgatcgg taaactacta ctc 93

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<211> 26

<212> DNA

<213> Artificial

<220>

<223> An artificially synthesized primer sequence

<400> 26

tagaattcca ccatggagtt tgggct 26

<210> 27
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 <212> DNA
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 <220>
 <223> An artificially synthesized primer sequence

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<210> 28
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<210> 29
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 <400> 29
 attgcggccg cttatcactt atcgtc 26

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 <212> DNA
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 <400> 30
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<210> 31
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 <212> DNA
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<400> 31
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<210> 32
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<400> 32
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<210> 33
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<220>
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<400> 33
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<210> 34
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<220>
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<210> 35
 <211> 36
 <212> DNA
 <213> Artificial

<220>
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<400> 35
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<210> 36
 <211> 12
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 <213> Artificial

<220>
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 <400> 36
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 1 5 10

 <210> 37
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 <220>
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 <220>
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 <210> 39
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 <400> 39
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 <210> 41

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